

NEW COMPOUNDS FROM HYPTIS. X-RAY CRYSTAL AND MOLECULAR  
STRUCTURES OF OLGUINE

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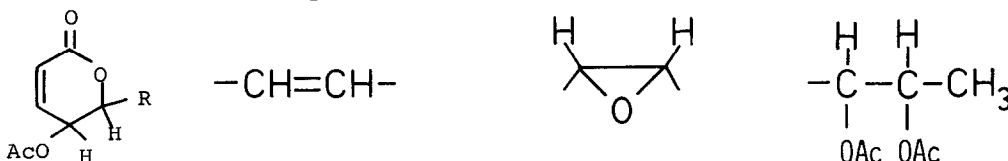
Summary. The structure (including absolute stereochemistry) of olguine, an unsaturated lactone isolated from an unclassified Hyptis species, has been established by spectroscopic and X-ray analysis.

Quite a few species of the Hyptis genus have been studied<sup>1</sup>. Among the components already reported are a hyptolide from H. pectinata leaves and a flavonoid glycoside from H. capitata<sup>1</sup>. Betulinic acid<sup>2</sup> and two other diterpenes of the abietane type - suaveolic acid and suavelol<sup>3</sup> - have also been isolated, from H. emoryi and H. suaveolens, respectively. Another diterpene of the same type has been isolated from H. fruticosa<sup>4</sup>. In this communication we report the isolation of two new compounds, olguine and anamarine, from an unclassified Hyptis species (Labiatae)<sup>5</sup>. The structure of olguine (1) is described here. That of anamarine will be the subject of another communication.

The flowers and leaves of this species were extracted with petroleum ether. On cooling, a mixture of oleanolic and ursolic acid separated. Further cooling yielded two other solid compounds. One of them, which we propose to name olguine (1), crystallized from CHCl<sub>3</sub>/CH<sub>3</sub>OH, m.p. 108-109°,  $[\alpha]_D^{20} +184^\circ$  (c,0.79,CHCl<sub>3</sub>). A second compound, which we propose to name anamarine, was purified by preparative tlc, m.p. 110-112°(CHCl<sub>3</sub>),  $[\alpha]_D^{20} +28.2^\circ$  (c,0.52,CHCl<sub>3</sub>). Both products showed UV absorption,  $\lambda_{\max}^{\text{EtOH}}$  220 nm ( $\epsilon$  2500).

Combustion analysis and mass spectrometry indicated the molecular formula C<sub>18</sub>H<sub>22</sub>O<sub>9</sub> for olguine (1). Its <sup>1</sup>H-NMR spectrum (CDCl<sub>3</sub>; see Fig. 1) showed three separate acetate signals. In addition, the <sup>1</sup>H-NMR spectrum revealed the presence of a sec-CH<sub>3</sub> group (3H, d,  $\delta$  1.20, J=6 Hz), two olefinic protons belonging to an  $\alpha,\beta$ -unsaturated carbonyl function ( $\delta$  6.20, d, J=10 Hz;  $\delta$  7.05, dd, J=10 Hz, J=6 Hz) and two other olefinic protons whose signals were centred at 5.80 ppm.

The  $^{13}\text{C}$ -NMR spectrum of olguine (1) confirmed the above results and provided new information. Carbonyl peaks could be observed at  $\delta 169.9$  (one acetate), 169.4 (two acetates) and 160.8. The latter chemical shift suggests an  $\alpha,\beta$ -unsaturated  $\delta$ -lactone<sup>6</sup>. Four olefinic carbon atom signals (doublets) appeared at  $\delta 140.1$ , 131.1, 126.6 and 124.7. The remaining seven peaks in this spectrum can be assigned to a methyl group ( $\delta 16.5$ , q), four trisubstituted carbon atoms, each one attached to an oxygen atom ( $\delta 74.6$ , 74.2, 69.7 and 62.5, d), and two tertiary epoxy carbon atoms ( $\delta 55.5$  and 54.5, d). Since the molecular formula is  $\text{C}_{18}\text{H}_{22}\text{O}_9$ , all the above requirements are fulfilled by the following partial structures :



- In order to establish the arrangement of these fragments, a series of decoupling experiments was carried out, which led to the following conclusions :
- 1) The proton at  $\delta 7.05$  (H-3, signal 9) is coupled to the proton at  $\delta 6.23$  (H-2,  $J_{23}=10$  Hz, signal 8) and to one of the protons at  $\delta 5.28$  (H-4,  $J_{34}=6$  Hz, signal 6).
  - 2) Proton H-4 at  $\delta 5.28$  shows a second coupling ( $J_{45}=3$  Hz) to the proton at  $\delta 4.20$ , which must be the lactonic hydrogen atom H-5.
  - 3) The latter (signal 4) exhibits another coupling ( $J_{46}=8$  Hz), namely to the proton at  $\delta 3.48$ , which must be one of the protons of the oxirane ring (H-6).
  - 4) The irradiation at the frequency of the other oxirane ring proton ( $\delta 3.65$ , signal 3) causes modifications in the signal at  $\delta 5.80$  (signal 7), assigned to two non-conjugated olefinic protons. There is a certain degree of sharpening as well as at the low field proton signal at  $\delta 5.34$ , implying a homoallylic coupling between H-7 and H-10.
  - 5) The proton at  $\delta 5.07$  (H-11, signal 5) is coupled to the methyl group.

On the basis of comparisons with similar compounds<sup>7</sup> and taking into account the factors affecting  $^{13}\text{C}$ -NMR chemical shifts, the  $^{13}\text{C}$ -NMR bands were assigned as follows: C-1 ( $\delta 160.8$ ), C-2 (124.7), C-3 (140.1), C-4 (62.5), C-5 (74.6), C-6 (55.5), C-7 (54.4), C-8 (126.6), C-9 (131.1), C-10 (74.2), C-11 (69.7), C-12 (16.5). A graphic correlation of a series of off-resonance proton-decoupled  $^{13}\text{C}$ -NMR spectra confirmed the above assignments for C-5, C-10 and C-11.

As a result of all the above spectroscopic data, the structure given in Fig. 1 is proposed for olguine. The mass spectrum of olguine showed a molecular ion at  $m/e$  382 and fragment ions at  $m/e$  280, 227, 185, 167, 155, 125, 113 and 95, which are consistent with the structure proposed.

As regards the stereochemistry, the value of  $J_{34}=6$  Hz suggests a quasi-equatorial configuration for H-4, which is confirmed by the lack of an observable allylic coupling of this proton to H-2. It seemed likely that the side chain also had a quasi-equatorial configuration, with H-5 axial. The CD curve showed a positive Cotton effect at 270 nm, suggesting<sup>8</sup> the stereochemistry depicted in Fig. 1,

later confirmed by an X-ray analysis which established furthermore the stereochemistry of the centres at the side chain.

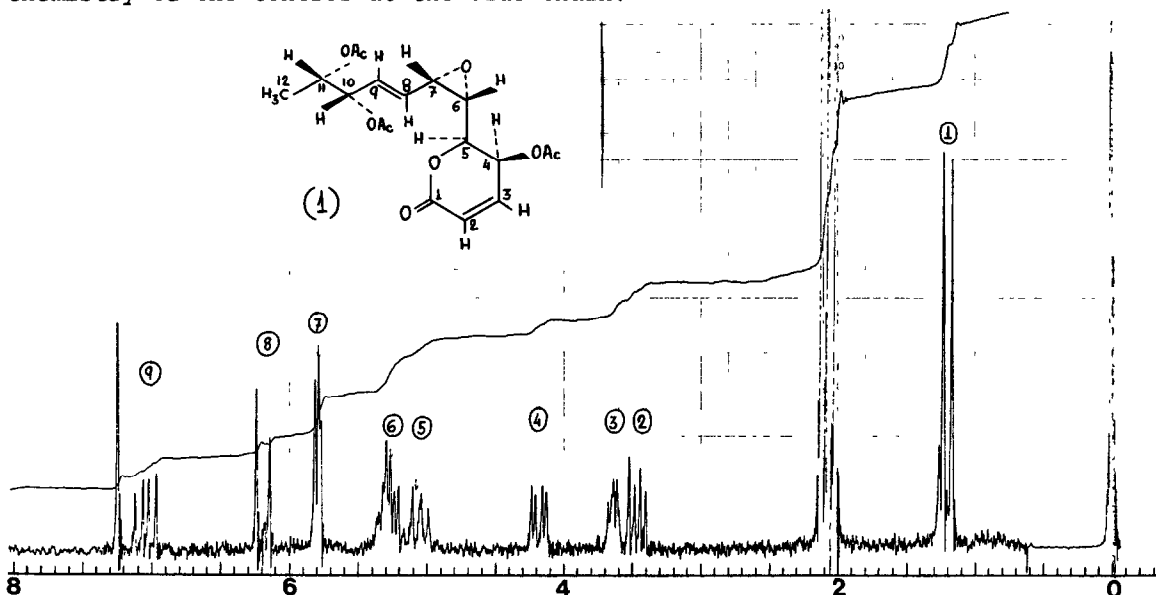
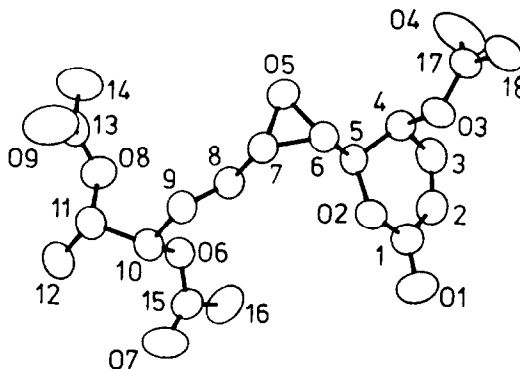


Fig. 1.  $^1\text{H}$ -NMR spectrum of olguine

A crystal fragment of  $0.2 \times 0.2 \times 0.3$  mm was used for the crystallographic study of olguine. The crystals were orthorhombic, space group  $P2_12_12_1$  with  $a=14.9309(3)$ ,  $b=12.3426(4)$ ,  $c=10.7215(2)$  Å,  $V=1975.8(1)$  Å<sup>3</sup>,  $D_c=1.28$  g cm<sup>-3</sup> and  $Z=4$ . 1,874 independent Friedel pairs were collected in the range  $2^\circ < \theta < 65^\circ$  using monochromated  $\text{CuK}_\alpha$  radiation. 1,621 Friedel pairs were considered observed by the criterion  $I > 2\sigma(I)$  and were used for the refinement of the structure. No absorption correction was applied. The structure was solved using the Multan package<sup>9</sup> and refined using the X-RAY 70 program system<sup>10</sup>. Atomic parameters were refined by full-matrix least-square analysis using anisotropic thermal coefficients for non-hydrogen atoms. The H atoms were located on a difference Fourier map, although some methyl H atoms had to be placed at the expected locations. A weighting scheme was applied in order to prevent bias on  $\langle w(F_o - F_c)^2 \rangle$  vs.  $\langle \sin\theta/\lambda \rangle$  and  $\langle F_o \rangle$ <sup>11</sup>. The final unweighted and weighted agreement factors were  $R=0.048$  and  $R_w=0.047$ . The absolute configuration of the molecule, shown in Fig. 2, was calculated using the anomalous dispersion effect of the oxygen atoms. The 65 more relevant Bijvoet pairs, those with  $F_o > 10\sigma(F_o)$ ,  $|\Delta|F_c|| > 0.14$  and  $|\Delta|F_o|| > 0.05$ , gave the following discrepancy indices,<sup>12</sup> average Bijvoet difference of 0.21 (0.41 for the reversal enantiomorph), average Bijvoet ratio of 0.04 (0.07) and  $\sum |\Delta F_o^2 - \Delta F_c^2| / \sum |\Delta F_o^2| = 0.69$  (1.69). This absolute configuration is the same as the one proposed for asperline<sup>13</sup>. The six-membered ring can be described as a distorted envelope, C5 being at the flap. The H atoms at the epoxy group are cis-configured.

Fig. 2. X-ray model of olguine, showing its absolute configuration.



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